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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,145	06/21/2005	Masatoshi Murai	44342.023000	5288

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EXAMINER	
CHOWDHURY, IQBAL HOSSAIN	
ART UNIT	**PAPER NUMBER**
1652	
MAIL DATE	**DELIVERY MODE**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,145	MURAI, MASATOSHI	
	Examiner	Art Unit	
	Iqbal H. Chowdhury, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-7,14-17,20 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-7, 14-17, 20-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application Status

In response to a previous Office action, a non-final requirement (mailed on January 30, 2007), Applicants filed a response and amendment received on May 24, 2007, amending claims 1, 3, 5-6, and adding new claims 20-21 is acknowledged. Claims 2, 11-13 and 18-19 are cancelled, and claims 8-10 are previously cancelled. Claims 1, 3-7, 14-17 and 20-21 are under consideration and will be examined herein.

Applicants' arguments filed on May 24, 2007, have been fully considered but are not deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Maintained-Claim Rejections - 35 USC § 112

Written Description requirement

Previous rejection of Claims 1, 3, 4, 7, 14, and 15 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained and new claims are included in this rejection. This rejection has been described at length in the previous Office action and it is maintained for the reasons of record and discussed below.

Claims are directed to a process for producing any PNPase, comprising constructing an expression vector comprising a PNPase gene integrated into a plasmid having a T7 promoter as an expression-regulating signal; transforming Escherichia coli or its analogous bacteria (part (A)) having a T7 RNA polymerase gene using the expression vector; allowing the resulting transformant to express the PNPase gene thereby accumulating PNPase in the bacteria; and

recovering the bacteria having PNPase accumulated therein, and extracting and purifying the PNPase.

Applicants argue that Claim 1 has been amended to recite that the expression vector comprises "a polynucleotide phosphorylase (PNPase) gene, which is isolated from a prokaryote selected from the group consisting of *Escherichia coli* and its analogous bacteria" and applicants believe this amendment is sufficient to overcome the written description rejection. Applicants also argue that the PNPases encoded by the PNPase genes isolated from *E. coli* and analogous bacteria such as *Salmonella typhimurium are* highly homologous to one another, probably more than 90% homologous. This is not found persuasive because claim 1 does not say that an analogous bacterium is Salmonella typhimurium. Applicants further state that one skilled in the art would reasonably conclude that the PNPases included within the scope of the presently claimed invention will behave, on the whole, in the same way as the PNPase, which is encoded by the PNPase gene isolated from the *E. coli* C 600K disclosed in the specification.

Applicant's arguments and amendments to claims have been fully considered but are not deemed to be persuasive to overcome the rejection on Written description issues.

Examiner acknowledges the amendment of claim 1, however the amendment does not give enough structural feature of any or all PNPase gene from any "analogous bacteria", which may include all gram negative bacteria, i.e. claim genus of any PNPase gene isolated from any analogous bacteria of E. coli, which is still substantially broad, therefore, the structural feature of the claimed genus can not be the representative of any PNPase gene from any analogous bacteria. As discussed in the written description guidelines the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of

species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species, which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus, one must describe a sufficient structure and variety of species to reflect the representative structure variation within the genus.** Satisfactory disclosure of a representative structure and number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of species disclosed. For inventions in an unpredictable art, adequate written description of a genus cannot be achieved by disclosing the structure of small portion of only one species within the genus. The genus of DNA from any analogous bacteria of E. coli is structurally diverse as it broadly encompasses many mutants, and variants having PNPase activity having different structures. As such, the disclosure solely of functional features coupled with minor structural feature that may or may not present in all members of the genus is insufficient to be representative of the attributes and features of the entire genus. Therefore, the rejection is maintained.

Enablement requirement

Previous rejection of Claims 1, 3, 4, 7, 14, and 15 rejected under 35 U.S.C. 112, first paragraph, on enablement issues is maintained and newly added claims are included in this

rejection. This rejection has been described at length in the previous Office action and it is maintained for the reasons of record and discussed below.

The specification, while being enabling for a process for producing a PNPase encoded by the PNP gene isolated from E. coli C600K, does not reasonably provide enablement for a process for producing any PNPase protein from any analogous bacteria of E. coli. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants argue that it is general common knowledge for a person of ordinary skill in the relevant art that the conserved regions in the PNPase are important to retain the catalytic activity, which is described in a reference ("Journal of Molecular Biology", vol. 321 (2002) pp. 397-409), wherein the reference shows the effect of various mutations inserted in the amino acids of *E. coli* PNPase, and almost all the mutations inserted to the phylogenetically conserved amino acids reduce the catalytic activity of PNPase. Applicants also argue that from the result, one skilled in the art can estimate that the mutations in the amino acids, which are little conserved do not affect the catalytic activity of PNPase. Therefore, such mutations are allowable. In addition, applicants further argue that it is natural that the amino acids in the transition regions between domains (e.g. first core domain, all--helical domain, second core domain, KH domain and S1 domain) are little conserved and can be also replaced or modified.

Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection. The examiner acknowledges the amendment to the claim 1 and reference but disagrees with the applicants' contention that the claimed invention is enabled for

full scope claimed. Claims are so broad as to encompass a process for producing any PNPase gene including mutants, and variants of E. coli or any analogous bacteria thereof. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of PNPase gene broadly encompassed by the claims.

The Examiner acknowledges regarding mutations in conserved or non-conserved region in relation to activity according to the reference, however, PNPase gene in any analogous bacteria might not behave similar to PNPase gene from E. coli. For example, Branden et al. (1991) teach that (1) protein engineers are frequently surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes, (2) the often surprising results obtained by experiments where single mutations are made reveal how little is known about the rules of protein stability, and (3) the difficulties in designing de novo stable proteins with specific functions. The teachings of Branden et al. are further supported by the teachings of Witkowski et al. (1999) and Seffernick et al. (2001), where it is shown that even small amino acid changes result in enzymatic activity changes. The specification clearly requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of PNPase gene from any analogous bacteria which may includes any gram negative bacteria, have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. As previously stated the applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a process for producing any PNPase from any analogous bacteria including any gram negative

bacteria. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of any PNPase to use in the claimed methods having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). Therefore, the rejection is maintained.

Maintained-Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Previous rejection of Claims 1, 3-7 and 11-19 under 35 U.S.C. 102(b) as being anticipated by Clements et al. (Polynucleotide phosphorylase is a global regulator of virulence and persistency in Salmonella enterica, Proc Natl Acad Sci U S A. 2002 Jun 25; 99(13): 8784-9 is maintained and claims 20-21 are included in this rejection.

Applicants argue that Claim 1 has been amended to incorporate the elements of claim 2 claim 1 now requires that expression continues until the bacteria is disrupted and the PNPase is recovered and purified from the supernatant and these limitations are not taught by Clements et al. Applicants further argue that since all of the remaining claims are dependent, directly or individually, from claim 1, these claims are also patentable over Clements et al.

Applicant's arguments have been considered but are not deemed persuasive to over come the rejection. Clements et al. indeed teach cloning in pET21(c) expression vector, expression in E. coli BL21 and purified as described by the manufacturer, wherein the process of Clements et al. inherently comprises disruption of cells for isolating the enzyme crude extract and recovering the purified PNPase. As discussed previously, Clements et al. teach the process for producing Salmonella PNPase and E. coli PNPase by constructing a vector comprising a prokaryotic PNPase encoding polynucleotide integrated in an expression vector pET30(c) having T7 promoter comprising regulatory sequence, T7 terminator having T7 tag and His Tag. Clements et al. further teach transformation of E. coli BL21 with the above vector followed by expression of PNPase protein in said E. coli as well as isolation and purification of protein according to a commercial protocol. Therefore, the rejection is also maintained as discussed.

Conclusion

Claims 1, 3-7, 14-17 and 20-21 are pending.

Claims 1, 3-7, 14-17 and 20-21 are rejected.

No claims are allowed.

Applicants must respond to the objections/rejections in each of the sections in this Office action to be fully responsive in prosecution. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R.

1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury, Ph.D. whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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